

APPENDIX A

PROPOSED COUNT

A method to activate expression of an endogenous gene in an isolated eukaryotic cell comprising, introducing a vector construct into said isolated eukaryotic cell, said vector construct comprising in operable combination

- 1) a promoter;
- 2) an exon sequence located 3' from and expressed by said promoter, said exon being derived from a naturally-occurring eukaryotic gene and not being a screenable marker gene; and
- 3) a splice donor sequence defining the 3' region of said exon said splice donor sequence being derived from a naturally-occurring eukaryotic gene;

wherein said vector construct is non-homologously incorporated into the genome of a said isolated eukaryotic cell and said splice donor sequence of the transcript encoded by said exon is spliced to a splice acceptor sequence of said endogenous gene.

- OR -

A method to alter expression of a gene in an isolated eukaryotic cell comprising introducing a 3' gene trap cassette vector into said cell, said 3' gene trap cassette vector comprising in operable combination

- 1) a promoter;
- 2) an exon sequence located 3' from and expressed by said promoter said exon being derived from a naturally-occurring eukaryotic gene said exon not encoding an activity conferring antibiotic resistance and said exon not being a reporter gene; and
- 3) a splice donor sequence defining the 3' region of said exon, said splice donor sequence being derived from a naturally occurring eukaryotic gene;

wherein said cassette is non-homologously incorporated into the genome of an eukaryotic target cell and said splice donor sequence of the transcript encoded by said exon is spliced to a splice acceptor sequence of said cellularly encoded gene.